In the Drawings:

A corrected drawing sheet in compliance with 37 CFR 1.121(d), reflecting the sequence identifier for Figure 1, is hereby submitted as a "Replacement Sheet" pursuant to 37 CFR 1.121(d).

REMARKS

Claims 1-14 are pending and stand rejected. Claims 1 and 8 have been amended.

I. In the Specification:

Applicants have amended the specification on page 1 to provide the priority information requested by the Examiner, specifically that "This application claims foreign priority to EP 02026342.2, filed November 22, 2002".

II. In the Drawings:

Applicants have amended the drawing sheet, labeled as "Replacement Sheet", to reflect sequence identifier for Figure 1 (Figure 1 corresponds to SEQ ID NO:1) in response to the Examiner's objection and in satisfaction of 37 C.F.R. 1.121(d). Accordingly, Applicants respectfully submit that the objection to the drawing has been obviated.

III. Claim Objection:

Claim 8 stands objected to for missing an article. Applicants have amended Claim 8 to reflect the missing article ("a") as suggested by the Examiner. Accordingly, Applicants respectfully submit that the claim objection to Claim 8 is now obviated and that said Claim 8 is now hereby placed into condition for allowance.

IV. Claim Rejections

A. 35 USC 112, first paragraph

Claims 8-14 stand rejected by the Examiner under 35 USC 112, first paragraph for lack of written description. Specifically, the Examiner contends that the claims encompass fragments and alleges that the specification does not demonstrate retention of function for the fragments to demonstrate possession of the genus as claimed in the invention. Applicants respectfully traverse.

Applicants note first of all for the record that the Examiner apparently meant to reject Claims 8-12 and 14 only under 35 USC 112, first paragraph. Claim 13 reflects the method of claim 1 with dosage/administration amount ranges of the human EPO protein. Claim 13 does not recite (or depend on a claim reciting) the "conjugate" terminology which is apparently the basis of the Examiner's rejection. Claims 8-12 and 14 do contain the phrase (or depend back to a claim reflecting the phrase) "wherein the erythropoietin protein is a conjugate" and thus these claims seem to be the focus of the Examiner's rejection under 35 USC 112, first paragraph. Accordingly, Applicants submit that Claim 13 is not rejected by 35 USC 112, first paragraph and thus as such stands in condition for allowance.

With regard to Claims 8-12 and 14, Applicants respectfully wish to point out that each claim specifically describes and identifies the analogs claimed, with reference to words, structures and formulae that fully set forth the claimed invention (*Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). In addition, each claim specifically sets forth the limit of said ranges for each of the component parts of the conjugate and its molecular weight and its activity. Support for these claims are found generally throughout Applicants' specification and specifically with regard to paragraphs 23-36 inclusive, and paragraphs 37-52 inclusive demonstrate and describe how to produce said conjugates as claimed. The Examiner acknowledges that the species are adequately described. As the species have included unpegylated and pegylated EPO, epoetin alfa or epoetin beta, 1-6 glycosylation sites and pegylated EPO with 1-6 glycosylation sites (as depicted in various formula in the specified paragraphs above, as well as methods for making same), applicants submit that the genus human EPO has been sufficiently described and disclosed in drawings/structural formula to show Applicant's possession of the claimed genus and thus also, the claimed invention.

B. 35 USC 112, second paragraph

1. Claims 3-14 apparently stand rejected for alleged failure to set forth and claim the subject matter which applicants regard as their invention. The Examiner has rejected claims 3-14 for lack of clear antecedent basis for "the erythropoietin protein" as original claim 1 recites "human erythropoietin".

Applicants have amended Claim 1 to reflect "human erythropoietin protein", thus providing antecedent support to Claims 3-14 and obviating the rejection. Accordingly, Applicants respectfully submit that claims 3-14 are now in condition for allowance.

2. Claims 8 and 11 stand additionally rejected for lack of clear antecedent basis for two reasons: first, the phrase "the erythropoietin protein is a conjugate" as original claim 1 recites "human erythropoietin" and second, the phrase "an erythropoietin protein" as this phrase allegedly reads on more than one protein/fragments which allegedly have no basis in original claim 1.

As noted above, Applicants have amended Claim 1 to reflect "human erythropoietin protein", thus providing antecedent support to Claims 8 and 11 and obviating the first ground of the rejection for these claims.

With regard to the second ground of the rejection, Applicants respectfully posit that both claims refer to an EPO protein which is then modified, this modification makes up the conjugate which is the EPO protein of claim 1. In other words, the EPO protein of claim 1 is in these claims a conjugate, the conjugate comprising an EPO protein + modifications. Accordingly, Applicants respectfully submit that the second ground of rejection to Claims 8 and 11 is inapposite and thus said claims are in condition for allowance.

C. 35 USC 102 (b)

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Silverberg et al. (Journal of the Amer. College of Cardiology, vol. 37, pages 1775-1780, June 1, 2000, (cited on IDS – July 28, 2005)). This rejection is traversed.

The Examiner contends that Silverberg et al., disclose a treatment method for anemia (disturbance of iron) in patients with congestive heart failure (CHF) (claim 2) by administering erythropoietin (EPO) and intravenous iron, (see page 1775 of the reference). The Examiner acknowledges that the reference does not explicitly teach epoetin alfa or beta, but contends these types are an inherent property of erythropoietin, as claim 3 recites the two types in the alternative.

As the Examiner acknowledges, Silverberg discloses treatment of anemia in patients with severe CHF by treatment with EPO and IV iron (Abstract background, Abstract methods, Abstract conclusions). No where does Silverberg address only treatment with EPO for this treatment.

In Applicants specification the term "disturbances of iron distribution" reflect conditions or states in which the overall concentration of iron in the body is normal, but distributed unequally (large amts in various organs, small amounts for incorporation into hemoglobin ("lowered concentration of hemoglobin in reticulocytes") and thus akin to anemic effects). See e.g., paragraphs 3-4, 10 of Applicant's specifications. Applicants' invention relates to those with chronic inflammatory intestinal diseases...who have normal amounts of iron but low concentration of hemoglobin (ie iron distribution disturbance) and treatment of these individuals with EPO, not EPO + iron. See e.g., paragraphs 5-6, 13 and rest of Applicant's specification.

Applicant's invention specifically warns against exceeding the normal overall concentration of iron in the body (paragraphs 2,3), which could possibly result. Thus, Silverberg fails as a 102(b) anticipatory reference, as it includes and requires an additional element (iron) in its method which is contrary to the teaching and claimed

method of Applicant's invention. Accordingly, Applicants respectfully submits that claims 1-3 are now in condition for allowance.

D. 35 USC 103(a)

1. Silverberg in view of Amgen and Hoffmann-La Roche

Claims 1-14 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Silverberg et al. (Journal of the Amer. College of Cardiology, vol. 37, pages 1775-1780, June 1, 2000, (cited on IDS – July 28, 2005)) in view of Amgen (EP 640619, March 1, 1995) and HOFFMANN-LA ROCHE (EP 1064 951, January 3, 2001 (cited on IDS – February 13, 2004).

The Examiner contends that Silverberg et al. disclose a treatment method for anemia (disturbance of iron) in patients with congestive heart failure (claim 2) by administering erythropoietin (EPO) and intravenous iron. The Examiner acknowledges that Silverberg et al. does not teach erythropoietin with modifications by adding 1 to 6 glycosylation sites, nor does Silverberg teach pegylated EPO. However, the Examiner contends that HOFFMANN-LA ROCHE teaches glycosylation of erythropoietin (see page 2 of the reference); and pegylated erythropoietin conjugates and the chemical structures claimed (see claim 4 and 7-15, pages 1-5 of the reference), and that it would have been obvious to one of ordinary skill in the art to combine the teachings of the references. The Examiner contends the modification would arise from the alleged teachings of Silverberg (erythropoietin is known in the art to treat anemia (iron disturbance) in patients) and HOFFMANN-LA ROCHE (teach erythropoietin for the same purpose and that as a conjugate to PEG an increased half-life is achieved). Applicants respectfully traverse.

As noted above, Silverberg at best teaches and requires EPO plus intravenous iron in its method treatment of inflammatory bowel disease. Silverberg therefore requires iron. Even if one skilled in the art was motivated to combine the Hoffmann-La

Roche EPO EP patent with Silverberg, there is no teaching to delete the required addition of iron in the Silverberg reference. As such, the combination of Silverberg and Hoffmann-La Roche do not teach Applicant's invention. Moreover, as Applicant's invention specifically warns against exceeding the normal level of iron concentration in the body, the combination of Silverberg and Hoffmann would teach away from Applicants invention as said combination would require concomitant addition of iron to those patients who suffer from IBS. Accordingly, as the cited references do not teach Applicants invention but actually teach away from same, Applicants respectfully submit that claims 1-14 as now presented are in condition for allowance.

2. Silverberg in view of Hoffmann-La Roche

Claims 1-14 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Silverberg et al. (Journal of the Amer. College of Cardiology, vol. 37, pages 1775-1780, June 1, 2000, (cited on IDS – July 28, 2005)) in view of Amgen (EP 640619, March 1, 1995) and HOFFMANN-LA ROCHE (EP 1064 951, January 3, 2001 (cited on IDS – February 13, 2004).

The Examiner contends that Silverberg et al. disclose a treatment method for anemia (disturbance of iron) in patients with congestive heart failure (claim 2) by administering erythropoietin (EPO) and intravenous iron. The Examiner acknowledges that Silverberg et al. does not teach erythropoietin with modifications by adding 1 to 6 glycosylation sites, nor does Silverberg teach pegylated EPO. However, the Examiner contends that HOFFMANN-LA ROCHE teaches glycosylation of erythropoietin (see page 2 of the reference); and pegylated erythropoietin conjugates and the chemical structures claimed (see claim 4 and 7-15, pages 1-5 of the reference), and that it would have been obvious to one of ordinary skill in the art to combine the teachings of the references. The Examiner contends the modification would arise from the alleged teachings of Silverberg (erythropoietin is known in the art to treat anemia (iron disturbance) in patients) and HOFFMANN-LA ROCHE (teach erythropoietin for the

same purpose and that as a conjugate to PEG an increased half-life is achieved). Applicants respectfully traverse.

As noted above, Silverberg at best teaches and requires EPO plus intravenous iron in its method treatment of inflammatory bowel disease. Silverberg therefore requires iron. Even if one skilled in the art was motivated to combine the Hoffmann-La Roche EPO EP patent with Silverberg, there is no teaching to delete the required addition of iron in the Silverberg reference. As such the combination of Silverberg and Hoffmann-La Roche do not teach Applicant's invention. Moreover, as Applicant's invention specifically warns against exceeding the normal level of iron concentration in the body, the combination of Silverberg and Hoffmann would teach away from Applicants invention as said combination would require concomitant addition of iron to those patients who suffer from IBS. Accordingly, as the cited references do not teach Applicants invention but actually teach away from same, Applicants respectfully submit that claims 1-14 as now presented are in condition for allowance.

E. The Double Patenting Rejection

1. Claims 1 and 3-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 3-12 of copending application USSN 10/634,477 (CD 21368). As claims 1 and 3-12 of USSN 10/634,477 are not allowed, applicants respectfully submit that this rejection is premature. Applicants request that the double patenting rejection be held in abeyance until there is an indication of allowability of the allegedly overlapping claims in both the instant case and USSN 10/634,477, at which point it can be assessed whether the allowed claims may in fact overlap. Without knowing what subject matter ultimately is allowed in both cases, applicants cannot fairly assess the propriety of the double patenting rejection. Applicants submit that if claims 1, and 3-14 of the instant application as well as certain claims 1 and 3-12 of USSN 10/634,477 are allowed in their current form, Applicants will tender a terminal disclaimer in the latest case that is allowed.

2. Claims 1 and 3-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 4-12 of copending application USSN 11/013,560. As claims 1 and 12 of USSN 11/013,560 are not allowed, applicants respectfully submit that this rejection is premature. Applicants request that the double patenting rejection be held in abeyance until there is an indication of allowability of the allegedly overlapping claims in both the instant case and USSN 11/013,560, at which point it can be assessed whether the allowed claims may in fact overlap. Without knowing what subject matter ultimately is allowed in both cases, applicants cannot fairly assess the propriety of the double patenting rejection. Applicants submit that if claims 1, and 3-14 of the instant application as well as certain claims 1 and 4-12 of USSN 11/013,560 are allowed in their current form, Applicants will tender a terminal disclaimer in the latest case that is allowed.

CONCLUSION

The foregoing amendment is fully responsive to the Office Action issued September 1, 2005. Applicants submit that claims 1-14, as amended, are allowable. Early and favorable consideration is earnestly solicited.

If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney is respectfully solicited.

No further fee is required in connection the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

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